UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,112	10/28/2003	Frank B. Gelder	VIR-021011CO01	4731

22876 7590 08/03/2009

FACTOR & LAKE, LTD
1327 W. WASHINGTON BLVD.
SUITE 5G/H
CHICAGO, IL 60607

EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
08/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/695,112	GELDER, FRANK B.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *159-220* is/are pending in the application.

4a) Of the above claim(s) *178,179,183-186 and 189-220* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *159-177,180-182,187 and 188* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/25/2007; 05/12/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Claims 159-220 are pending in the instant application. Acknowledgement is hereby made of receipt and entry of the communication filed 30 November, 2005, wherein Group I (claims 159-177, 180-182, 187, and 188) was elected with traverse. Applicant argues that the Office failed to provide adequate support for the restriction of Groups 1-32 (see items (i)-(vii) in the response). It was further noted that claim 159 is a genus claim linking all of the aforementioned inventions. Upon the allowability of said linking claim, the restriction requirement between the linked inventions should be withdrawn. See M.P.E.P. § 809. Finally, it was concluded that an undue burden would not be required if all the groups were examined concomitantly. Applicant's arguments have been carefully considered but are note deemed to be persuasive. The basis for the restriction requirement was clearly provided and explained in the Office action mailed 28 July, 2005 (reproduced again below). Adequate support was clearly set forth for the various groups identified (see pages 6-8 below). Applicant's comments pertaining to the presence of a linking claim are noted. Finally, an undue burden is clearly present because separate searches would be required for each invention. For example, a search of amino acids 4-27 of HIV gp120 would not be coextensive with a search of amino acids 254-295 of HIV RT. Clearly there is a substantial burden present.

37 C.F.R. § 1.142

The following is a quotation of 37 C.F.R. § 1.142:

(a) If two or more independent and distinct inventions are claimed in a single application, the examiner in an Office action will require the applicant in the reply to that action to elect an invention to which the claims will be restricted, this official action being called a requirement for restriction (also known as a requirement for division). Such requirement will normally be made before any action on the merits; however, it **may be made at any time before final action.**
(b) Claims to the invention or inventions not elected, if not canceled, are nevertheless withdrawn from further consideration by the examiner by the election, subject however to reinstatement in the event the requirement for restriction is withdrawn or overruled.

35 U.S.C. § 121

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

a. Group I, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to **amino acids 4-27 of HIV gp120**, classified in class 424, subclass 188.1.

b. Group II, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to **amino acids 54-76 of HIV gp120**, classified in class 424, subclass 188.1.

c. Group III, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to **amino acids 502-541 of HIV gp41**, classified in class 424, subclass 188.1.

d. Group IV, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to **amino acids 254-295 of HIV RT (p66/55)**, classified in class 424, subclass 188.1.

e. Group V, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to **amino acids 69-94 of HIV PR (p10)**, classified in class 424, subclass 188.1.

f. Group VI, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to **amino acids 166-181 of HIV CA (p24)**, classified in class 424, subclass 188.1.

g. Group VII, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to amino acids 390-410 of HIV NC (p7), classified in class 424, subclass 188.1.

h. Group VIII, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to amino acids 438-443 of HIV NC (p7), classified in class 424, subclass 188.1.

i. Group IX, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to amino acids 2-23 of HIV MA (p17), classified in class 424, subclass 188.1.

j. Group X, claim(s) 159-177, 180-182, 187, and 188, drawn to a vaccine composition comprising a viral polypeptide corresponding to amino acids 89-122 of HIV MA (p17), classified in class 424, subclass 188.1.

k. Group XI, claim(s) 159-174, 178, 179, 180-182, 187, and 188, drawn to a vaccine composition comprising a deglycosylated HIV gp120, classified in class 424, subclass 208.1.

l. Group XII, claim(s) 159-174, 178, 179, 180-182, 187, and 188, drawn to a vaccine composition comprising a deglycosylated HIV gp41, classified in class 424, subclass 208.1.

m. Group XIII, claim(s) 159-174, 178, 179, 180-182, 187, and 188, drawn to a vaccine composition comprising a deglycosylated HIV CA (p24), classified in class 424, subclass 208.1.

n. Group XIV, claim(s) 159-174, 178, 179, 180-182, 187, and 188, drawn to a vaccine composition comprising a deglycosylated HIV NC (p7), classified in class 424, subclass 208.1.

o. Group XV, claim(s) 159-174, 178, 179, 180-182, 187, and 188, drawn to a vaccine composition comprising a deglycosylated HIV PR (p10), classified in class 424, subclass 208.1.

p. Group XVI, claim(s) 159-174, 178, 179, 180-182, 187, and 188, drawn to a vaccine composition comprising a deglycosylated HIV RT (p66/55), classified in class 424, subclass 208.1.

q. Group XVII, claim(s) 159 and 183, drawn to a vaccine composition comprising a combination of multiple viral immunogens, classified in class 424, subclass 202.1.

r. Group XVIII, claim(s) 159, 185, and 186, drawn to a vaccine composition comprising a an epitope that corresponds to human α-fetal protein, classified in class 424, subclass 184.1.

s. Group XIX, claim(s) 159, 185, and 186, drawn to a vaccine composition comprising a an epitope that corresponds to **aspartyl protease**, classified in class 424, subclass 184.1.

t. Group XX, claim(s) 159, 185, and 186, drawn to a vaccine composition comprising a an epitope that corresponds to **deoxyuridine-triphosphate nucleotidohydrolase**, classified in class 424, subclass 184.1.

u. Group XXI, claim(s) 159, 185, and 186, drawn to a vaccine composition comprising a an epitope that corresponds to **eosinophil cationic protein**, classified in class 424, subclass 184.1.

v. Group XXII, claim(s) 159, 185, and 186, drawn to a vaccine composition comprising a an epitope that corresponds to **eosinophil-derived neurotoxin**, classified in class 424, subclass 184.1.

w. Group XXIII, claim(s) 159, 185, and 186, drawn to a vaccine composition comprising a an epitope that corresponds to a **ribonuclease-4-precursor**, classified in class 424, subclass 184.1.

x. Group XXIV, claim(s) 189-196, drawn to a vaccine composition comprising a **nucleic acid** encoding a modified **Gag** polypeptide, classified in class 536, subclass 23.72.

y. Group XXV, claim(s) 189-196, drawn to a vaccine composition comprising a **nucleic acid** encoding a modified **Pol** polypeptide, classified in class 536, subclass 23.72.

z. Group XXVI, claim(s) 189-196, drawn to a vaccine composition comprising a **nucleic acid** encoding a modified **Env** polypeptide, classified in class 536, subclass 23.72.

aa. Group XXVII, claim(s) 197-208, drawn to a vaccination **method** employing a modified **Gag** polypeptide, classified in class 424, subclass 208.1.

bb. Group XXVIII, claim(s) 197-208, drawn to a vaccination **method** employing a modified **Pol** polypeptide, classified in class 424, subclass 208.1.

cc. Group XXIX, claim(s) 197-208, drawn to a vaccination **method** employing a modified **Env** polypeptide, classified in class 424, subclass 208.1.

dd. Group XXX, claim(s) 209-220, drawn to a vaccination **method** employing a **nucleic acid** encoding a modified **Gag** polypeptide, classified in class 536, subclass 23.72.

ee. Group XXXI, claim(s) 209-220, drawn to a vaccination method employing a nucleic acid encoding a modified Pol polypeptide, classified in class 536, subclass 23.72.

ff. Group XXXII, claim(s) 209-220, drawn to a vaccination method employing a nucleic acid encoding a modified Env polypeptide, classified in class 536, subclass 23.72.

The inventions are distinct, each from the other because of the following reasons:

Inventions 1-23 are all unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, each group is directed toward a structurally and functionally different polypeptide (e.g., aa 4-27 of HIV gp120, aa 502-541 of HIV gp41, aa 390-410 of HIV NC, human α-fetal protein, etc.). The modified polypeptides do not share any common structural features and will all necessitate independent searches. Accordingly, each identified group is clearly directed toward a different inventive concept.

Inventions 24-26 are all are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, each of the nucleic acids is directed toward a structurally and functionally different structural region (e.g., Gag, Pol, or Env). The modified nucleotides do not share any common structural features and will all necessitate independent searches. Accordingly, each identified group is clearly directed toward a different inventive concept.

Inventions 1-23 and 24-26 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation,

different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, each group is directed toward structurally and functionally different macromolecules (e.g., proteins or nucleic acids). Since the various groups do not share a common structural feature, separate searches will be required for each group. Clearly, each identified group is directed toward a different inventive entity.

Inventions 27-29 and 30-32 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, each group is directed toward a methodology that employs structurally and functionally different reagents (e.g., polypeptide vaccines, nucleic acid vaccines). Clearly, each group is directed toward a different inventive concept.

Inventions 1-23 and 30-32 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, the methodologies of groups 30-32 neither require nor utilize the compounds of groups 1-23.

Inventions 24-26 and 27-29 are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (M.P.E.P. § 806.04 and § 808.01). In the instant case, the methodologies of groups 27-29 neither require nor utilize the nucleic acids of groups 24-26.

Inventions 1-23 and 27-29 are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, each of the modified viral polypeptides can be employed in a materially different methodology such as affinity purification or enzymatic assays.

Inventions 24-26 and 30-32 are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the nucleic acids of groups 24-26 can be used in a materially different process such as hybridizaiton assays to detect virus.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, recognized divergent subject matter, and require separate searches, restriction for examination purposes as indicated is proper.

Accordingly, restriction for examination purposes as indicated was proper because all these inventions listed are independent or distinct for the reasons given above and there

would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. § 101 and/or 35 U.S.C. § 112, first paragraph.

Accordingly, the requirement is still deemed proper and is therefore made **FINAL**. Claims 178, 179, 183-186, and 189-220 are withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

37 C.F.R. § 1.98

The information disclosure statements filed 25 May, 2007, and 12 May, 2008, have been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 159-177, 180-182, 187, and 188 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are broadly directed toward a vaccine composition comprising a modified viral polypeptide, wherein the modified viral polypeptide corresponds to a naturally-occurring viral polypeptide that is non-immunogenic in a subject but immunogenic in a non-subject. Thus, the claims appear to be directed toward a mimotope that unduces a humoral immune response against a cryptic or silent epitope. The term vaccine has an art-recognized meaning and refers to a composition with therapeutic or prophylactic properties.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity

of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The state-of-the-art vis-à-vis HIV vaccine development has been characterized by repeated failure (Desrosiers, 2004; Burton, 2004; Gallo, 2005; Walker and Burton, 2008). Several factors have contributed to the lack of success including the following: 1) The quasispecies nature of HIV infection leads to rapid immune evasion and escape due to neutralization resistance. 2) HIV is capable of down-regulating major histocompatibility class I (MHC) molecules from the surface of infected cells thereby rendering them resistant to CTL-mediated cytolysis. 3) HIV selectively targets and destroys $CD4^+$ T-helper cells thereby hampering the ability of the immune system to mount a meaningful response. 4) Current animal models are not predictive of clinical efficacy. 5) The correlates of human protection remain to be elucidated. 6) The appropriate immunogen(s), formulations, adjuvants, routes of administration, and immunization regimens that will lead to a protective or therapeutic outcome remain to be elucidated. 7) HIV is capable of integrating into the host's chromosome where it may actively replicate or enter a quiescent phase. Thus, any given immune response will need to maintain high titers of neutralizing activity.

2) The disclosure fails to provide adequate guidance pertaining to the identification of suitable mimotopes. Which modified viral polypeptides are capable of inducing an immune response in one subject but not another? Does the immunoreactivity vary within the same species (i.e., due to MHC differences) or is it due to cross-species variations?

3) The disclosure fails to provide adequate guidance pertaining to the subject responsiveness toward any given mimotope.

4) The disclosure fails to provide adequate guidance pertaining to the identification of suitable amino acid additions, deletions, or substitutions that will create a mimotope with the desired properties (see claim 160). It has been well-documented that single amino acid substitutions, additions, or deletions can abrogate antigen-antibody binding and the immunogenicity of a polypeptide. It is not readily manifest which viral targets should be employed and how they should be modified in such a manner that they retain the desired activities.

5) The disclosure fails to provide adequate guidance pertaining to the identification of suitable regions of genetic relatedness that are required for the activity of any given mimotope (see claim 161).

6) The disclosure fails to provide adequate guidance pertaining to the hydrophobicity/hydrophilicity profile of any given mimotope and which modifications will produce a peptide with the desired activity.

7) The broadest claims encompass an inordinate number of modified viral polypeptides and are not limited to any particular virus or protein. The claims could encompass polypeptides from virtually any viral family and subfamily.

8) The disclosure fails to provide any working embodiments. Considering the unpredictability of the prior art, a working embodiment demonstrating the modified polypeptide could induce a therapeutic or prophylactic response would be required.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention. Applicants may obviate the rejection by directing the claim language toward an "immunogenic composition" comprising the desired modified viral polypeptide. Applicant's representative may wish to contact the Examiner to discuss the application further to facilitate compact prosecution.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Larry R. Helms, can be reached at (571) 272-0832. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile

Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

17 July, 2009